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Title of the Invention: Semiconductor Element for Detecting Organic Molecules, Semiconductor Device for Detecting Organic Molecules, and Method for Measuring Organic Molecules Using Same

Claims

[Claim 1] A semiconductor element for detecting organic molecules, characterized in that a photoelectric converter is disposed on a first main side of a semiconductor substrate, and an organic molecule probe disposition region is formed on a second main side.

[Claim 2] A semiconductor element for detecting organic molecules as defined in Claim 1, characterized in that an optical filter is formed on the second main side, at least at the location corresponding to the organic molecule probe disposition region.

[Claim 3] A semiconductor element for detecting organic molecules as defined in Claim 1 or 2, characterized in that the thickness of the semiconductor substrate, from the organic molecule probe disposition region on the second main side to the photoelectric converter on the first main side, is determined according to the depth of a CCD potential well.

[Claim 4] A semiconductor device for detecting organic molecules, characterized in that a plurality of photoelectric converters are disposed on a first main side of a semiconductor substrate, and organic molecule probe disposition regions are provided on a second main side, corresponding at least to the photoelectric converters.

[Claim 5] A semiconductor device for detecting organic molecules as defined in Claim 4, characterized in that a photoelectric converter region in which a plurality of the photoelectric converters are disposed is formed on the first main side, and the second main side serves as the side where light is incident, constituting a CCD solid-state imaging device.

[Claim 6] A semiconductor device for detecting organic molecules as defined in Claim 4 or 5, characterized in that an optical filter is formed in at least the organic molecule probe disposition region on the second main side.

[Claim 7] A semiconductor device for detecting organic molecules as defined in any of Claims 4 to 6, characterized in that a plurality of recesses corresponding to the organic molecule probe disposition region are provided on the second main side.

[Claim 8] A method for measuring organic molecules using a semiconductor device as defined in any of Claims 4 to 7, characterized by comprising:

a step of fixing at least one type of organic molecule probe in the organic molecule probe disposition region on the second main side;

a step of pouring a fluorescent-labeled sample onto the second main side and bonding a target having a molecular structure corresponding to the organic molecule probe included in said sample to said organic molecule probe;

a step of irradiating the second main side to which the organic molecule probe has been fixed with excitation light; and

a step of detecting the fluorescent light produced by irradiation with the excitation light by means of the photoelectric converters disposed on the first main side, and outputting an optical signal.

[Claim 9] A method for measuring organic molecules as defined in Claim 8, characterized in that organic molecule probes with different molecular structures in each region are fixed to the plurality of organic molecule probe disposition regions disposed on the second main side.

Detailed Description of the Invention

[0001]

Technological Field to Which the Invention Belongs

The present invention relates to an organic molecule detecting semiconductor element and an organic molecule detecting semiconductor device, which are used to detect a target such as DNA, mRNA, or protein with a specific molecular structure, and to an organic molecule measurement method. More particularly, it relates to an organic molecule detecting semiconductor element and an organic molecule detecting semiconductor device that combine a substrate on which a DNA probe, mRNA probe, or protein probe is fixed, and a substrate of a solid-state imaging element or solid-state imaging device for capturing images of a target, and to an organic molecule measurement method that makes use of these.

[0002]

Prior Art

Techniques for analyzing the DNA structure of plants and animals have been developed in recent years, such as those used in the Human Genome Project. Of the semiconductor devices used to detect organic molecules, a DNA chip in particular is known as a semiconductor device that is used for detecting organic molecules in order to analyze DNA structures.

[0003]

With this DNA chip, a DNA probe (organic molecule probe) having a base sequence (molecular structure) corresponding to the base sequence of the target DNA is fixed on a substrate such as a slide glass. A sample containing the target DNA is then poured onto this substrate, the above-mentioned DNA probe is complementarily bound to the DNA having the specified structure (the above-mentioned base sequence) out of all the DNA contained in the sample, and this bound DNA is optically detected with a microscope, solid-state imaging device, or the like.

[0004]

The sample here first undergoes a treatment in which it is fluorescent labeled, and a DNA probe having the corresponding base sequence is complementarily bound by a hybridization treatment or the like to fix [the sample] onto the substrate. When this fluorescent label is irradiated with excitation light having a specific wavelength (short

wavelength), such as ultraviolet rays, the fluorescent label emits light (fluorescent light), and this fluorescent light is optically detected, which indicates which DNA probe it is bound to.

[0005]

Methods for fixing a DNA probe to a substrate include chemically synthesizing a specific DNA base sequence, and spotting a substrate with natural DNA.

The former involves utilizing semiconductor photolithography to chemically synthesize a DNA probe of a specific base sequence on the surface of a substrate (glass substrate). The latter involves spotting a substrate (slide glass, nylon sheet, etc.) with DNA of a specific structure extracted from natural DNA that serves as an indicator, and fixing [the DNA] to the substrate. With both of these methods, several types of DNA probe are generally fixed at specific locations on a single chip (the DNA probe disposition region).

[0006]

Meanwhile, the DNA of the specified structure (target) contained in the sample is extracted from the specimen and poured onto the surface of a DNA chip after undergoing treatment such as proliferation or fluorescent labeling. As a result, if DNA of the specified structure (target) is contained in the sample, it is complementarily bound to the DNA probe of the corresponding base sequence (hybridization). After this, the unnecessary sample is removed from the substrate, leaving only the complementarily bound DNA on the substrate. This DNA is fluorescent labeled.

[0007]

Because this hybridized DNA of the specified structure (target) has been fluorescent labeled, when the substrate is irradiated with excitation light such as UV rays, the fluorescent label emits light, which can be optically measured (with a microscope or solid-state imaging device, for instance).

In particular, to detect DNA of a specific structure that is complementarily bound to a DNA probe, a DNA probe of the specified structure may be fixed to the surface (incident side) of a substrate (semiconductor substrate) of a CCD solid-state imaging device, and this DNA probe may be detected, which eliminates the need to use an expensive optical system such as a microscope, making this method useful for DNA analysis.

[0008]

A DNA chip with which DNA of a specific structure can be detected, in which a DNA probe of a specific structure is disposed on the incident side (semiconductor substrate surface) of a CCD solid-state imaging device, is known from U.S. Patent 5,846,708, for example.

Fig. 11 illustrates a conventional DNA chip (organic molecule detecting semiconductor device) 10. This organic molecule detecting semiconductor device 10 has a photoelectric converter 12 formed on a silicon substrate 11, and recesses 16 are formed in a silicon oxide film 13 formed over this. DNA probes 21 are fixed in these recesses 16.

[0009]

With the organic molecule detecting semiconductor device 10 structured as above, an interline (IT) method is employed as one transfer method for reading out the electrons photoelectrically converted on the side where the excitation light is incident (the incident side) to an external circuit.

This interline (IT) type of CCD solid-state imaging device is structured such that electrodes 14 are disposed on the incident side, and the fluorescent light emitted from the fluorescent label is detected by the underlying photoelectric converter 12.

[0010]

Problems Which the Invention is Intended to Solve

However, with the CCD solid-state imaging device 10 [sic] having a conventional IT design in which DNA probes are disposed on the incident side, since the incident side is the side of the silicon substrate 11 on which the electrodes 14 are formed, the aperture area is lowered in proportion to the disposition of the electrodes 14. Increasing the aperture area becomes particularly difficult as the size of the element is reduced.

[0011]

Furthermore, the following problem may be encountered with the conventional organic molecule detecting semiconductor device 10 in which DNA probes of a specific structure are fixed on the incident side.

A chemical treatment with an organic substance is performed repeatedly with the above-mentioned method, in which a DNA base sequence is chemically synthesized on a substrate.

Chemicals that are rarely used in the manufacture of semiconductors are used in large quantities in these organic chemical treatments. The purity of these chemicals is high enough to synthesize a DNA base sequence, but generally not high enough to satisfy the purity (EL) requirements of semiconductor manufacturing technology.

[0012]

Consequently, if chemicals are used to synthesize a DNA base sequence on the surface of a silicon substrate on which solid-state imaging elements constituting a single pixel are formed, the effect of impurities contained in these chemicals could possibly diminish the performance of the solid-state imaging elements, so that it may not be possible to accurately detect the very faint fluorescent light produced from the target.

The present invention was conceived in light of this situation, and it is an object thereof to provide a semiconductor element for detecting organic molecules and a semiconductor device for detecting organic molecules, which afford higher sensitivity and better durability with respect to synthetic treatment of organic molecule probes, and to provide a method for measuring organic molecules in which these are used.

[0013]

Means Used to Solve the Above-Mentioned Problems

To solve the above problems, the semiconductor element for detecting organic molecules according to Claim 1 is such that a photoelectric converter is disposed on a first main side of a semiconductor substrate, and an organic molecule probe disposition region is formed on a second main side. This constitution eliminates the need to separately provide an optical system for reading the light produced from the target during analysis of organic molecules such as DNA, so the overall apparatus used for analysis of organic molecules is more compact and the manufacturing costs are lower. Also, since the photoelectric converters formed by semiconductor manufacturing technology and the organic molecule probes formed by organic chemical treatment are formed on mutually different sides, the effect that the impurities in the chemicals used in the formation of the organic molecule probe would have on the photoelectric converter is eliminated.

[0014]

The semiconductor element for detecting organic molecules according to Claim 2 is such that an optical filter is formed on the second main side, at least at the location corresponding to the organic molecule probe disposition region. In a measurement method in which fluorescent labels are attached to organic molecules with the specified structure, and these labels are irradiated with excitation light to generate fluorescent light, the above-mentioned optical filter cuts out the excitation light and only transmits the generated fluorescent light, so it is possible to measure this fluorescent light while irradiating with the excitation light, which means that analysis of the organic molecules with the specified structure takes less time.

[0015]

The semiconductor element for detecting organic molecules according to Claim 3 is such that the thickness of the semiconductor substrate, from the organic molecule probe disposition region on the second main side to the photoelectric converter on the first main side, is determined according to the depth of a CCD potential well. If the thickness of the semiconductor substrate is reduced while still ensuring enough thickness to form potential wells, the electrons by the fluorescent light on the second main side can be detected by the photoelectric converter on the first main side.

[0016]

The semiconductor device for detecting organic molecules according to Claim 4 is such that a plurality of photoelectric converters are disposed on a first main side of a semiconductor substrate, and organic molecule probe disposition regions are provided on a second main side, corresponding at least to the photoelectric converters. This constitution eliminates the need to separately provide an optical system for reading the light produced from the target during analysis of organic molecules such as DNA, so the overall apparatus used for analysis of organic molecules is more compact and the manufacturing costs are lower. Also, since the photoelectric converter formed by semiconductor manufacturing technology and the organic molecule probe formed by organic chemical treatment are formed on mutually different sides, the effect that the impurities in the chemicals used in the formation of the organic molecule probe would have on the photoelectric converter is eliminated.

[0017]

The semiconductor device for detecting organic molecules according to Claim 5 is such that a photoelectric converter region in which a plurality of the photoelectric converters are disposed is formed on the first main side, and the second main side serves as the side where light is incident, constituting a CCD solid-state imaging device. As a result, it is possible, for example, to configure a frame transfer type of CCD solid-state imaging device in which the light is incident on the back side, so the aperture area is higher (80% or higher). This increase in aperture area raises the sensitivity of the solid-state imaging device, allowing the very faint fluorescent light generated from the organic molecule probes to be measured.

[0018]

The semiconductor device for detecting organic molecules according to Claim 6 is such that an optical filter is formed in at least the organic molecule probe disposition region on the second main side. In a measurement method in which fluorescent labels are attached to organic molecules with the specified structure, and these labels are irradiated with excitation light to generate fluorescent light, the above-mentioned optical filter cuts out the excitation light and only transmits the generated fluorescent light, so it is possible to measure this fluorescent light while irradiating with the excitation light, which means that analysis of the organic molecules with the specified structure takes less time.

[0019]

The semiconductor device for detecting organic molecules according to Claim 7 is such that a plurality of recesses corresponding to the organic molecule probe disposition region are provided on the second main side. This makes the spotting with the organic molecules of the specified structure easier and more certain.

The method for measuring organic molecules according to Claim 8 makes use of the semiconductor device in any of Claims 4 to 7, wherein said measurement method comprises a step of fixing at least one type of organic molecule probe in the organic molecule probe disposition region on the second main side, a step of pouring a fluorescent-labeled sample onto the second main side and bonding a target having a molecular structure corresponding to the organic molecule probe included in said sample to said organic molecule probe, a step of irradiating the second main side to which the organic molecule probe has been fixed with excitation light, and a step of detecting the fluorescent light produced by irradiation with the excitation light by means of the photoelectric converters disposed on the first main side, and outputting an optical signal.

[0020]

The measurement method according to Claim 9 is such that organic molecule probes with different molecular structures in each region are fixed to the plurality of organic molecule probe disposition regions disposed on the second main side. Since organic molecule probes with different molecular structures are fixed in each region (corresponding to a unit pixel), it is possible to detect a plurality of different types of target DNA with a single treatment.

[0021]

Embodiments of the Invention

First Embodiment

A first embodiment of the present invention will now be described through reference to Figs. 1 to 8.

The organic molecule detecting semiconductor device 100 in this embodiment is an FT type of CCD solid-state imaging device, in which numerous pixels 110 [each] having a photoelectric converter are provided. A single pixel 110 here corresponds to a single solid-state imaging element.

[0022]

Numerous recesses 112 are formed on the back side (the second main side) 101B of a silicon substrate 101, corresponding to the pixels 110 having photoelectric converters. An optical filter/DNA fixing film 114 is formed at the bottom of these recesses 112. In this embodiment, the bottom of the recesses 112 serves as the organic molecule probe disposition region for fixing the organic molecule probes (the DNA probes 161 in this case).

[0023]

The thickness d1 of the silicon substrate 101 down to the bottom of the recesses 112 is about 10 to 20 μm. This thickness d1 is determined according to the depth of the potential wells of the pixels 110.

The optical filter/DNA fixing film 114 formed at the bottom of the recesses 112 cuts out excitation light and transmits fluorescent light. Also, the optical filter/DNA fixing film 114 is positioned between the pixels 110 (including their photoelectric converters) and the DNA probes 161, and this optical filter/DNA fixing film 114 makes it possible to measure the fluorescent light from the DNA probes during irradiation with the excitation light (such as ultraviolet rays) in the course of measuring the DNA 172 with a specific structure (see Fig. 5) bound to the DNA probes 161.

[0024]

As shown in Fig. 2, this organic molecule detecting semiconductor device 100 is housed in a ceramic package 150. The electrodes 116 of the organic molecule detecting semiconductor device 100 here are electrically connected by bumps 152 to electrodes 151 on the package 150 side. The organic molecule detecting semiconductor device 100 and the package 150 are bonded together in a water-tight seal with a resin adhesive agent 156.

[0025]

Fig. 3 shows the simplified circuit structure of the organic molecule detecting semiconductor device 100. As shown in this drawing, the organic molecule detecting semiconductor device 100 is an FT type of CCD solid-state imaging device in which the light is incident on the back side, and the main side (the 101B side of the second main side) is divided into a photoelectric converter region 131 and an accumulator 132. With this organic molecule detecting semiconductor device 100, the optical signal obtained at the various pixels 110 in the photoelectric converter region 131 is transferred to the accumulator 132 by drive current (such as four-phase drive current) from a terminal 136,

after which this signal is outputted through a horizontal reader 133 and an amplifier 134 and from an output terminal 135 to the outside.

[0026]

This organic molecule detecting semiconductor device 100 that constitutes a back side-incident FT type of CCD solid-state imaging device affords a high aperture area (80% or higher), and is therefore favorable for detecting very faint fluorescent light from the DNA 172 (Fig. 5), whose specific structure will be discussed in detail below.

The organic molecule detecting semiconductor device 100 thus configured is a back side-incident CCD solid-state imaging device, and frame transfer (FT) is used as the transfer method for reading the electrons photoelectrically converted on the incident side (the rear side). Because a back side-incident CCD solid-state imaging device has no electrodes or the like formed on the incident side, and because the pixel region (including the photoelectric converters) is the same as the transfer region, the aperture area can be greater than with other solid-state imaging devices.

[0027]

Therefore, with the organic molecule detecting semiconductor device 100, as will be discussed in detail below, it is possible to detect the very faint fluorescent light generated when fluorescent labeled DNA is irradiated with short wavelength light such as ultraviolet rays.

Also, with the organic molecule detecting semiconductor device 100, the semiconductor substrate (silicon substrate) 101 at the bottom of the recesses 112 consists of a thin film about 10 to 20 μm in thickness, so short wavelength light with a large absorption coefficient is almost completely absorbed and converted into electrons in the vicinity of the incident side (back side), and there is a low probability that these electrons will disappear through rebonding within the substrate by the time they reach the pixels (including the photoelectric converters), which would lower the sensitivity, or that the electrons produced by light incident at different places on the incident side will become admixed, which would lower the resolution.

[0028]

Next, a DNA measurement method in which the organic molecule detecting semiconductor device 100 is used will be briefly described through reference to Figs. 4 and 5.

With the organic molecule detecting semiconductor device 100 structured as above, DNA probes 161 are fixed by spotting at the bottom of the recesses 112 formed on the surface of the organic molecule detecting semiconductor device 100 (the organic molecule probe disposition region) (Fig. 4a and Fig. 5a). The recesses 112 here are formed corresponding to the various pixels 110. As described in detail below, DNA probes with different base sequences from a DNA library are fixed at the bottom of these recesses.

[0029]

Also, because the organic molecule probe disposition region is at the bottom of the recesses 112 with the organic molecule detecting semiconductor device 100, spotting is favorable.

As a result of the above treatment, the DNA probes 161 having base sequences of the specified structure are fixed in the organic molecule probe disposition region (at the bottom of the recesses 112 in this embodiment).

[0030]

Meanwhile, the DNA (target) 172 of the specified structure contained in the sample is extracted from the specimen and subjecting to treatment such as proliferation or fluorescent labeling (Fig. 5b).

After this, the sample containing the DNA (target) 172 of the specified structure is poured onto the incident side (side 101B) of the organic molecule detecting semiconductor device 100 (Fig. 4b).

If the DNA (target) 172 of the specified structure corresponding to the DNA probes 161 is contained in the sample at this point, as shown in Fig. 5c, complementary binding occurs between the DNA probes 161 and the DNA 172 of the specified structure, and when the extra sample is washed, such as by washing it with water, the fluorescent labeled DNA 172 of the specified structure remains on the incident side (side 101B) of the organic molecule detecting semiconductor device 100.

[0031]

In this state, the incident side (side 101B) of the organic molecule detecting semiconductor device 100 is irradiated with excitation light (such as UV rays) while the signals from the pixels 110 are read.

In this case, because the optical filter/DNA fixing film 114 is provided to the bottom of the recesses 112 formed on the incident side (side 101B) of the organic molecule detecting semiconductor device 100 (the organic molecule probe disposition region), the excitation light can be cut out in the course of measuring the fluorescent light of the DNA (target) 172 of the specified structure by selecting a wavelength of light that can be cut. As a result, fluorescent light from the DNA (target) 172 of the specified structure can be measured during irradiation with excitation light, which means that the DNA measurement takes less time.

[0032]

Next, a method for manufacturing the organic molecule detecting semiconductor device 100 will be described through reference to Figs. 6 and 7. What will be described here is chiefly the method for manufacturing the pixels 110 on the 101A side (first main side) of the organic molecule detecting semiconductor device 100, and the recesses 112 on the 101B side (second main side). Therefore, a detailed description will not be given of the methods for manufacturing the other peripheral circuits, impurity diffusion regions, interlayer insulation films between wiring, and so forth of the organic molecule detecting semiconductor device 100.

[0033]

The first step in manufacturing the organic molecule detecting semiconductor device 100 is to form an epitaxial layer (silicon epitaxial growth layer) 102, in which p-type impurities have been introduced at a low concentration (about 1×10^{14} cm^{-3}), in the desired thickness using an epitaxial growth apparatus, over the top of a silicon substrate in which p-type impurities have been introduced at a high concentration (about 1×10^{20} cm^{-3}).

[0034]

Next, a silicon oxide film 103 that constitutes a gate oxide film, and electrodes (transfer electrodes with a two-layer structure) 104 composed of polysilicon and which serve as the charge transfer component are formed over the epitaxial layer 102. Over this is formed an insulating silicon oxide film (passivation film) 105 such as PSG (phosphosilicate glass) or BPSG (borophosphosilicate glass), forming pixels (including photoelectric converters) 110 on the front (first main side) 101A of the silicon substrate 101. Fig. 6a shows the structure of the device obtained in the steps so far.

[0035]

Next, a glass substrate 106 is bonded with a resin-based adhesive (such as a silicon-based adhesive) to the surface of the silicon oxide film 105 (Fig. 6b).

The rear (second main side) 101B of the silicon substrate 101 is then lapped and polished (mechanical polishing) to the required film thickness using a polishing apparatus. Fig. 7c shows the structure of the device obtained in the steps so far.

[0036]

The recesses 112 are then formed by dry etching, for instance, on the rear (second main side) 101B of the silicon substrate 101. During the formation of the recesses 112, the rear (second main side) 101B is coated with an etching resist (not shown in the drawings), and this etching resist is positioned so that the apertures thereof line up with the pixels 110 on the front (first main side) 101A on the front and back of the silicon substrate 101. As a result, the pixels 110 on the front (first main side) 101A correspond with the bottoms (organic molecule probe disposition region) of the recesses 112 on the rear (second main side) 101B.

[0037]

In the formation of the recesses 112, the etching is continued until the thickness d1 of the silicon substrate 101 at the bottom of the recesses 112 is about 10 to 20 μm. This thickness d1 ensures that adequate potential wells will be formed. Wet etching may also be performed in the formation of the recesses 112. If it is, a silicon nitride film may be formed ahead of time on the rear (second main side) 101B, and this film patterned as used as a mask. The thickness d1 of the silicon substrate 101 can be controlled more easily by preforming a stopper layer.

[0038]

Next, a p^+ region 112A is formed by the injection of boron at the bottom of the recesses 112 (the organic molecule probe disposition region). This p^+ region 112A serves to prevent electrons from being trapped, and allows light to be detected at higher sensitivity (high-sensitivity treatment). The injection of boron for this high-sensitivity

treatment may be performed over the entire rear (second main side) 101B. Instead of injecting boron, a thin platinum film (0.001 to 0.002 μm, for example) may be formed for the purpose of this high-sensitivity treatment. Fig. 7d shows the structure of the device obtained in the steps so far.

[0039]

Next, a multilayer film 113 that doubles as an optical filter that transmits fluorescent light and cuts out UV rays and as a glass substrate on which the DNA probes 161 can be fixed is formed so as to cover the entire rear (second main side) 101B.

This multilayer film 113 has, for example, a three-layer structure consisting of a silicon oxide film at the top, an aluminum oxide film in the middle, and a magnesium oxide film at the bottom, and is designed to cut out light of a specific wavelength (not shown in the drawings). As long as the uppermost layer of this multilayer film 113 is a film to which the DNA probes 161 can be fixed (such as a silicon oxide film), there are no restrictions on the material of the other films. Specifically, an aluminum oxide film, magnesium oxide film, titanium oxide film, or the like should be suitably laminated so as to function as a filter for cutting out light of the specified wavelength. The thickness of the films is determined as dictated by the wavelength of the light to be cut. The multilayer film 113 may instead comprise only two layers, or it may comprise four or more layers. Fig. 7e shows the structure of the device obtained in the steps so far.

[0040]

Finally, patterning is performed so as to leave the multilayer film 113 only at the bottom of the recesses 112 (the organic molecule probe disposition region), which yields the organic molecule detecting semiconductor device 100 with the structure shown in Fig. 1.

In measuring the DNA of the specified structure, the organic molecule detecting semiconductor device 100 structured as above is subjected to saponification with sodium hydroxide or the like, and to a coating treatment with poly-L-lysine or the like, so that the DNA probes 161 will be fixed more securely to the optical filter/DNA fixing film 114.

[0041]

Here, since the front (first main side) 101A of the silicon substrate 101 is protected by the glass substrate 106, the peripheral circuits of the pixels 110 and so forth are not contaminated by these chemicals.

[0042]

Also, because the optical filter/DNA fixing film 114 remains only at the bottom of the recesses 112 (the organic molecule probe disposition region) as mentioned above, the DNA probes 161 are prevented from adhering to other regions where they are not needed.

If the precision of the spotting of the DNA probes 161 (see Fig. 5) is high, the optical filter/DNA fixing film may be left over the entire rear (second main side) 101B of the silicon substrate 101, without patterning the multilayer film 113.

[0043]

Fig. 8 is an oblique view schematically illustrating the organic molecule detecting semiconductor device 100. (a) is the rear (second main side) 101B, while (b) is the front (first main side) 101A.

As shown in the drawings, numerous pixels 110 having photoelectric converters (which also double as readers) are disposed on the rear (second main side) 101B, forming an FT type of CCD solid-state imaging device (photoelectric converter region 131), and forming the accumulator 132 for accumulating the signal charges sent from the pixels 110 of the photoelectric converter region 131.

[0044]

The horizontal reader 133 and the amplifier 134 are connected to this accumulator 132. Numerous pads 138 for inputting drive current or outputting optical signals are disposed around the periphery of the photoelectric converter region 131 and the accumulator 132.

Here, that portion of the front (first main side) 101A corresponding to where the recesses 112 are disposed on the rear (second main side) 101B corresponds to the photoelectric converter region 131. Since no recesses 112 are disposed in the portion corresponding to the accumulator 132 here, a signal processing circuit 180 that is electrically connected to the various circuits is disposed in this portion.

[0045]

The signal processing circuit 180 may also be disposed on the front (first main side) 101A. Further, the above-mentioned numerous pads 138 may be disposed on the rear (second main side) 101B.

The signal processing circuit 180 must be shielded from light so that photoelectric conversion does not occur where not desired as a result of incident light. In thus shielding the signal processing circuit 180 from light, a light blocking film may, for example, be formed so as to cover the signal processing circuit 180 portion of the front (first main side) 101A of the silicon substrate 101, or the signal processing circuit 180 portion may be covered with the package 150 (see Fig. 2).

[0046]

In the first embodiment given above, the description was of an example in which the DNA probes were fixed by spotting at the bottom of the recesses 112 the organic molecule probe disposition region), but the DNA probes may also be synthesized by semiconductor photolithography in this organic molecule probe disposition region.

Also, in the first embodiment given above, the description was of an example in which a single recess 112 was provided corresponding to a single pixel 110, but a single recess 112 may also be provided corresponding to a plurality of pixels 110.

[0047]

Second Embodiment

The organic molecule detecting semiconductor device 200 of a second embodiment of the present invention will now be described through reference to Figs. 9 and 10.

As shown in Fig. 9, the organic molecule detecting semiconductor device 200 in this second embodiment is an organic molecule detecting semiconductor device of a type in which the DNA probes are chemically synthesized on the incident side (second main side) 201B of a silicon substrate 201, and therefore, the difference from the organic molecule detecting semiconductor device 100 in the first embodiment given above is that no spotting recesses are provided on the rear (second main side) 201B. The rest of the structure is the same as that of the organic molecule detecting semiconductor device 100 in the first embodiment, and will therefore not be described in detail.

[0048]

The organic molecule detecting semiconductor device 200 of this second embodiment is also a frame transfer (FT) type of CCD solid-state imaging device (see Fig. 3). As a result, the detection sensitivity for fluorescent light produced when fluorescent labeled DNA is irradiated with short-wavelength light such as UV rays is again increased with the organic molecule detecting semiconductor device 200.

[0049]

With this organic molecule detecting semiconductor device 200, the semiconductor substrate (silicon substrate) 201 consists of a thin film about 10 to 20 μm in thickness, which makes it easier for the electrons generated in the vicinity of the incident side (back side) to reach the light receiving elements (diffusion layer, electrodes, etc.) on the front.

In view of this, as shown in Fig. 9, the DNA probes 161 are fixed by synthesizing them in a specific region of the rear (second main side) 201B (at places corresponding to the pixels 210 on the front 201A). In this case, as shown in the drawings, the fixed DNA probes 161 can be different in each region corresponding to the pixels 210 (161a to 161d).

[0050]

An optical filter/DNA fixing film 214 is formed over the entire surface of the rear (second main side) 201B, which is the incident side. This optical filter/DNA fixing film 214 makes it possible to measure the fluorescent light from the DNA probes 161a to 161d during irradiation with the excitation light (such as ultraviolet rays) in the course of measuring the DNA 172 (172a to 172d) with a specific structure.

[0051]

With this organic molecule detecting semiconductor device 200 of the second embodiment, there is no need for an optical system for reading the fluorescent light from the DNA (target) 172 of the specified structure, so the overall apparatus required for analysis of DNA of the specified structure is more compact.

A method for manufacturing the organic molecule detecting semiconductor device 200 will now be described through reference to Fig. 10.

[0052]

Fig. 10a illustrates the step conducted after the manufacturing step of the first embodiment (Fig. 7c).

The organic molecule detecting semiconductor device 200 is applied mainly to a DNA measurement method in which the DNA probes 161 are chemically synthesized, so the rear (second main side) 201B is flat, and the silicon substrate 201 is etched to a thickness d2 of 10 to 20 μm.

[0053]

Next, a multilayer film (the optical filter/DNA fixing film 214) that doubles as an optical filter that transmits fluorescent light and cuts out UV rays and as a film on which the DNA probes 161 can be fixed is formed so as to cover the entire rear (second main side) 201B. This optical filter/DNA fixing film 214 has the same structure as in the first embodiment. Fig. 10b shows the structure of the device obtained in the steps so far.

[0054]

As shown in Fig. 9, the organic molecule detecting semiconductor device 200 structured as above is housed in a ceramic package 150.

In this second embodiment, the description was of an example in which the DNA probes were formed by chemically synthesizing base sequences on the rear (second main side) 201B, but the rear (second main side) 201B may also be spotted with natural DNA. In this case, since no recesses 112 are formed as they were with the organic molecule detecting semiconductor device 100 in the first embodiment, if the optical filter/DNA fixing film 214 is formed only the portions corresponding to the pixels 210, then the DNA probes 161 can be fixed at just these portions during spotting. Here, during the patterning of the optical filter/DNA fixing film 214, it should be accurately aligned with the pixels 210 on the front (first main side) 201A.

[0055]

As described above, the organic molecule detecting semiconductor devices 100 and 200 in the first and second embodiments are each a back-incident frame transfer type of CCD solid-state imaging device, so the region where the DNA probes are disposed can be completely isolated from the region where the signal processing component is formed.

As a result, every time DNA of the specified structure is detected on the rear (second main side) of the organic molecule detecting semiconductor devices 100 and 200 where the DNA probes are fixed, the corresponding DNA probes can be removed by chemical treatment (treatment with stripping chemicals) and the other DNA probes refixed, which makes it possible to measure the DNA of the specified structure by the repeated use of the organic molecule detecting semiconductor devices 100 and 200.

[0056]

Also, in the first and second embodiments given above, the description was of an example in which the DNA probes 161 were fixed to the rear sides (second main sides) 101B and 201B of the organic molecule detecting semiconductor devices 100 and 200 in order to detect the DNA of the specified structure, but other organic molecule probes may also be fixed, such as mRNA probes, or protein probes, and the organic molecule detecting semiconductor devices 100 and 200 may be used in the measurement of the mRNA, protein, or the like of the specified structure.

[0057]

Also, the above embodiments were examples of using a frame transfer type of CCD solid-state imaging device as the organic molecule detecting semiconductor devices 100 and 200, but the present invention can also be applied to a CMOS solid-state imaging device or other device as long as it is a back-incident type of solid-state imaging device.

It should go without saying that a so-called full-frame transfer type of solid-state imaging device is encompassed by the above-mentioned frame transfer type of solid-state imaging device.

[0058]

Effect of the Invention

As described above, with the invention pertaining to Claim 1 or 4, there is no need to separately provide an optical system for reading the light produced from the target during analysis of organic molecules such as DNA, so the overall apparatus used for analysis of organic molecules is more compact and the manufacturing costs are lower. Also, since the photoelectric converter formed by semiconductor manufacturing technology and the organic molecule probe formed by organic chemical treatment are formed on mutually different sides, the effect that the impurities in the chemicals used in the formation of the organic molecule probe would have on the photoelectric converter is eliminated.

[0059]

With the invention pertaining to Claim 2 or 6, it is possible to measure fluorescent light while irradiating with excitation light, which means that analysis of the organic molecules (such as DNA) with the specified structure takes less time.

With the invention pertaining to Claim 3, when a CCD is used for charge transfer, the electrons produced on the incident side can be detected at high sensitivity by the photoelectric converter on the first main side while ensuring the thickness required for the formation of potential wells.

[0060]

With the invention pertaining to Claim 5, a back-incident frame transfer type of CCD solid-state imaging device is constituted, so the aperture area is higher (80% or higher), and the very faint fluorescent light produced from the organic molecule probe can be measured at good sensitivity.

The invention pertaining to Claim 7 makes spotting easier and more certain.

[0061]

With the invention pertaining to Claim 8, analysis of organic molecule of a specific structure can be performed at high sensitivity and in a short time.

With the invention pertaining to Claim 9, organic molecule probes of different base sequences are fixed, so it is possible to detect a plurality of types of target (DNA) with a single process.

Brief Description of the Drawings

Fig. 1 is a cross section of the organic molecule detecting semiconductor device 100 in the first embodiment;

Fig. 2 is a diagram of the organic molecule detecting semiconductor device 100 of the first embodiment when housed in the package 150;

Fig. 3 is a simplified block diagram of the structure of the organic molecule detecting semiconductor device 100 of the first embodiment;

Fig. 4 consists of diagrams illustrating how DNA is analyzed using the organic molecule detecting semiconductor device 100 of the first embodiment;

Fig. 5 consists of detail diagrams illustrating how DNA is analyzed using the organic molecule detecting semiconductor device 100 of the first embodiment;

Fig. 6 consists of cross sections illustrating the steps of manufacturing the organic molecule detecting semiconductor device 100 of the first embodiment;

Fig. 7 consists of cross sections illustrating the steps of manufacturing the organic molecule detecting semiconductor device 100 of the first embodiment;

Fig. 8 consists of oblique views schematically illustrating the organic molecule detecting semiconductor device 100 of the first embodiment;

Fig. 9 is a diagram of the organic molecule detecting semiconductor device 200 of the second embodiment when housed in the package 150;

Fig. 10 consists of cross sections illustrating the steps of manufacturing the organic molecule detecting semiconductor device 200 of the second embodiment; and

Fig. 11 is a cross section of a conventional organic molecule detecting semiconductor device 10.

Key:

100, 200 organic molecule detecting semiconductor device

101, 201 silicon substrate (semiconductor substrate)

101A, 201A first main side (front)

101B, 201B second main side (rear)

110, 210 pixels

112 recesses

114, 214 optical filter/DNA fixing film

161 DNA probes (organic molecule probes)

172 DNA (target)

Document Title: Figures

Fig. 1

Fig. 2

Fig. 3

Fig. 4

Fig. 5

Fig. 6

Fig. 7

Fig. 8

132 (accumulator)

131 (photoelectric converter region)

Fig. 9

Fig. 10

Fig. 11 (transfer direction)

Document Title: Abstract

Abstract

Object: To provide a semiconductor device for detecting organic molecules, which affords higher sensitivity and better durability with respect to synthetic treatment of organic molecule probes.

Means for Solution: An organic molecule detecting semiconductor device 100 has pixels (including photoelectric converters) 110 disposed on the front (first main side) 101A of a silicon substrate 101, and recesses 112 (the bottoms of which serve as the organic molecule probe disposition region) in which DNA probes 161 are fixed are formed on the rear (second main side) 101B. The organic molecule detecting semiconductor device 100 constitutes a back-incident FT type of CCD solid-state imaging device. In the analysis of DNA or other organic molecules, there is no need for the separate provision of an optical system for reading the light produced from the target (DNA of the specified structure). The overall apparatus is more compact and the manufacturing costs are reduced. Also, the pixels 110 formed by semiconductor manufacturing technology and the DNA probes 161 formed by organic chemical treatment are formed on mutually different sides.

Selected Figure: Fig. 1